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REMARKS/ARGUMENTS

Pending claims 27-41 are presented, hereby, in place of claims 12-26, cancelled hereby without prejudice or disclaimer.

Present claims 27-37 and 41 represent claims 12-17 and 21-23, respectively, revised to more clearly define the invention and, thereby, resolve rejections of record, as further explained below.

The rejections of record under 35 USC 112, ¶1, 35 USC 112, ¶2, and 35 USC 102(b) as applied against claims 24-26 are rendered moot by cancellation of the rejected claims, hereby.

Claims 12-23 were rejected under (1) 35 USC 112, ¶2, for allegedly being indefinite, (2) 35 USC 112, ¶1, for allegedly containing *new matter*, and under (3) 35 USC 112, ¶1, for allegedly lacking enablement. Reconsideration of the aforesaid §112 rejections of record is requested.

First, reconsideration is requested in that the rejection applies the wrong standard (test) for determining satisfaction of the requirements under §112, ¶2. According to the statement of rejection, the claims are indefinite for not reciting "How . . . the chemosensitivity of cells is determined" (Office Action, page 2). The statement of rejection confuses the function of the claims, on the one hand, with the function of the specification, on the other.

"*How*" the claimed invention is practiced is the function of the "specification," *not* the claims, the function of which is to *define the legal limits* of the invention. *In re Roberts*, 176 USPQ 313, 315 (CCPA 1973). Therefore, the §112, ¶2, rejection is in order for withdrawal, at least to the extent it concerns the procedure by which (i.e., *how*) "the chemosensitivity of cells is determined" in accordance with the invention claimed.

Secondly, the present claims reflect revising of the rejected to expressly include a "fluorogenic substrate comprising the sequence motif DEVD" for measuring caspase activity. Apart from some changes of rather minor nature, applicant submits that the language of independent claim 12 is amended hereby, as claim 27, to include a "fluorogenic substrate comprising the sequence motif DEVD" for measuring caspase activity, as indicated above. Accordingly, the allegations (i.e., reasoning) supporting the §112 rejections with respect to *a genus caspase substrate* do not apply to the present claims, since other *fluorogenic substrates comprising the sequence motif DEVD* are well known to one of ordinary skill in the art, e.g., as amply demonstrated by the cited references Benjamin et al. and Martins et al., of record. In satisfying the requirements of §112, ¶1, "an application need not teach, and preferably omits, that which is well known in the art." *Staehelin v. Secher*, 24 USPQ2d 1513, 1516 (BPA & I 1992).

Claims 12-23 were rejected under 35 USC 102(b) for allegedly lacking novelty based on each of Benjamin et al. and Martins et al. Reconsideration is requested.

For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp.* To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis*

added). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

At least the following claim limitation of the present claims (recited in independent claim 27) is absent from each of Benjamin et al. and Martins et al.:

> measuring the accumulated caspase activity in the sample without previously separating off the cells

On the contrary, Benjamin et al. teach to wash the cells twice after treatment with etoposide (see left column of page 447 titled "Experimental procedures - Protease assay"). This means that the cells are separated from the surrounding medium because the medium is washed away. Consequently, any caspase activity present in the medium is washed away and cannot contribute anymore to measuring the "accumulated caspase activity" in the sample (the sample comprising cells and medium according to the language of the present claims).

Martins et al. also separate off the cells, i.e.: "Cells were treated with 17 μmol/L etoposide for 1 hour, sedimented at 150*g* for 10 minutes, and resuspended in drug-free medium A or B, respectively" (Martins, page 4284, right hand column, ¶ headed "*Induction of apoptosis*"). In other words, the cells were sedimented and the cell precipitate was resuspended into a fresh medium. As such, any caspase activity present in the original medium can no longer contribute to measuring the "accumulated caspase activity," i.e., because the cells are separated from such medium before the caspase activity is measured upon complete lysis of the cells.

Each of Benjamin et al. and Martins et al. teaches one skilled in the art to be in a position to measure, merely, a fraction of the complete caspase activity induced by the addition of a substance.

Cells undergoing apoptosis show characteristic biochemical and morphological features. These characteristics include the partition of cytoplasm and nucleus into membrane bound vesicles, so-called apoptotic bodies. Such apoptotic bodies undergo "secondary necrosis," which is associated with swelling and partial lysis of the vesicles. Conducting an apoptose assay in a way as described in either of the cited references bears the risk that cells have already started to undergo secondary necrosis, with a concomitant release of caspase activity in the medium before the cells are separated from the medium. Consequently, any caspase activity released into the medium due to the presence of the test substance is not detected in accordance with the separation process taught in either of the cited references.

In contrast to the lack of detecting any caspase activity released into the medium due to the presence of the test substance, as in the cited references, the presently claimed invention teaches *not* to separate off the cells. Therefore, the presently claimed invention allows measuring the full effect a test substance has on the cellular apoptotic process, i.e., measuring the complete accumulated caspase activity, even if secondary necrosis has already occurred. Neither cited references teaches (or, even, suggests) such a procedure.

Conducting an assay in accordance with the presently claimed invention is advantageous because (i) the results are not biased, which happens as a consequence of the separation taught by the cited references, and (ii) the assay performed in accordance with the present claims is of a homogeneous nature and, therefore, feasible for the automation employed, especially, in high-

throughput processes, such as conducted in the search for new chemotherapeutics or in monitoring samples from patients undergoing a chemotherapy.

Accordingly, there being at least one limitation on the present claims absent from each of the cited references, anticipation of the present claims under §102(b) based on either of the cited references is negated. *Kolster Speedsteel A B, supra.* Applicant submits that the rejection of record under 35 USC 102(b) based on each of Martins et al. and Benjamin et al. is inapplicable against present claims 27-41.

Request for Acknowledgment of Foreign Priority Under 35 USC 119

A claim to foreign priority under 35 USC 119 has been made (inventorship declaration, filed April 16, 2001), and the certified copies of the two (German) priority documents, sent by the International Bureau, received by the PTO (Notification of Acceptance, mailed April 30, 2001, by the PTO, and Form PCT/IB304, mailed 12 July 2000 by the International Bureau).

The Office Action mailed October 17, 2002 (Office Action Summary page, item 13), was marked to indicate "None" of the certified copies of the priority documents had been received by the PTO. The Office Action was marked incorrectly, in this respect.

The instant application represents the U.S. national stage of international application PCT/EP00/02174 and, therefore, 35 USC 365(b) is controlling with respect to the §119 priority claim. As such, filing certified copies of the two (German) priority documents with the International Bureau, as in the present case, satisfies the requirements for obtaining priority under section 119. As set forth in MPEP 201.13(b), i.e. (*emphasis added*):

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201.13(b) Right of Priority Based upon an International Application Filed under the Patent Cooperation Treaty

. . . 35 U.S.C. 365(b) provides that an international application designating the United States shall be entitled to the right of priority of . . . a regularly filed foreign application. . . An international application which seeks to establish the right of priority will have to comply with the . . . the requirement of . . . *submitting a certified copy of the priority document to the International Bureau* at a certain time (Rule 17 of the PCT Regulations). The submission of the priority document to the International Bureau is only required in those instances where priority is based on an earlier filed foreign national application.

Accordingly, the examiner is asked to mark the next Office Action to acknowledge the §119 priority claim to *both* German patent applications *and* to acknowledge receipt of the corresponding certified copies; with attention being directed, in particularly, to marking item 13(a)(3) of "Office Action Summary" (form PTO-326), which acknowledges receiving: "Copies of the certified copies . . . in this National Stage application from the International Bureau."

Favorable action is requested.

Respectfully submitted,

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